Introduction

THE ROLE OF GENETICS IN MEDICINE

Genetics as a Medical Specialty

This is an especially exciting time in medical and human genetics. Medical genetics has achieved a recognized role as the specialty of medicine that deals with the diagnosis, treatment, and management of hereditary disorders. The idea that medical genetics is concerned only with the inheritance of trivial, superficial, and rare characteristics has given way to an understanding of the fundamental role of the gene in basic life processes. Medical and human geneticists are at the forefront of investigations into human variability and human heredity while also participating in and benefiting from rapid progress in molecular biology, biochemistry, and cell biology. In particular, the last decade of the 20th century and the beginning of the 21st century have seen the initiation of the Human Genome Project, an international effort to determine the complete content of the human genome, defined simply as the sum total of the genetic information of our species, encoded within each nucleated cell of the body. In partnership with all the other disciplines of modern biology, the Human Genome Project is already revolutionizing human and medical genetics by providing fundamental insights into many diseases and promoting the development of far better diagnostic tools, preventive measures, and therapeutic methods in the near future. When completed, the Human Genome Project will make available the complete sequence of all human DNA; knowledge of the complete sequence will, in turn, allow the identification of all human genes and, ultimately, make it possible to determine how variation in these genes contributes to health and disease.

Relevance of Genetics to All Medical Practice

Although medical genetics has become a recognized specialty, it has also become abundantly clear that human genetics provides important unifying concepts that illuminate and unify all medical practice. To give patients and their families the full benefit of expanding genetic knowledge, all physicians and their colleagues in the health professions need to understand the underlying principles of human genetics. The existence of alternative forms of a gene (alleles) in the population; the occurrence of similar phenotypes developing from mutation and variation at different loci; the importance of gene-gene and gene-environmental interactions in disease; the role of somatic mutation in cancer and aging; the feasibility of prenatal diagnosis, presymptomatic testing, and population screening; and the promise of powerful gene therapies are concepts that now permeate all medical practice and will become only more important in the future. Thus, genetic principles and approaches are not restricted to any one medical subspecialty.

One aspect of medical genetics practice relevant to all of medicine deserves special emphasis: it focuses not only on the patient but also on the entire family. A comprehensive family history is an important first step in the analysis of any disorder, whether or not the disorder is known to be genetic. As pointed out by Childs, “to fail to take a good family history is bad medicine. . . .” A family history is important because it can be critical in diagnosis, may show that a disorder is hereditary, can provide information about the natural history of a disease and variation in its expression, and can clarify the pattern of inheritance. The diagnosis of a hereditary condition allows the risk in other family members to be estimated, so that proper management, prevention, and counseling can be offered to the patient and the family.

Disciplines within Human and Medical Genetics

Genetics is a diverse subject concerned with variation and heredity in all living organisms. Within this broad field, human genetics is the science of variation and heredity in human beings, whereas medical
**GENETICS** deals with the subset of human genetic variation that is of significance in the practice of medicine and in medical research.

Within human and medical genetics, there are many fields of interest, as indicated by the various directions in which genetics has developed. Major recognized areas of specialization are the study of chromosomes (cytogenetics); the study of the structure and function of individual genes (molecular and biochemical genetics); the study of the genome, its organization, and functions (genomics); the study of genetic variation in human populations and the factors that determine allele frequencies (population genetics); the study of the genetic control of development (developmental genetics); and the application of genetics to diagnosis and patient care (clinical genetics). The literal meaning of clinical is bedside (klinikos, Greek for “bedside”), and a clinical geneticist is an appropriately qualified physician-geneticist directly involved in the diagnosis of genetic diseases and the care of patients with such diseases. Genetic counseling, which combines the provision of risk information while providing psychological and educational support, has matured into a new health profession with a whole cadre of genetic professionals dedicated to the care of patients and their families.

In addition to direct patient contact, medical geneticists provide care to individuals, through the provision of laboratory diagnosis, and to the population at large, through screening programs designed to identify persons at risk of developing or transmitting a genetic disorder. The diagnosis of genetic disease in patients, carrier testing, prenatal diagnosis, and the identification of individuals at risk of developing disease later in life are rapidly expanding specialties in clinical laboratories. Population screening for genetic disease is also becoming increasingly widespread.

**CLASSIFICATION OF GENETIC DISORDERS**

In clinical practice, the chief significance of genetics is in elucidating the role of genetic variation and mutation in the etiology of a large number of disorders. Virtually any disease is the result of the combined action of genes and environment, but the relative role of the genetic component may be large or small.

Among disorders caused wholly or partly by genetic factors, three main types are recognized:

1. Single-gene disorders
2. Chromosome disorders
3. Multifactorial disorders

**Single-gene defects** are caused by individual mutant genes. The mutation may be present on only one chromosome of a pair (matched with a normal allele on the homologous chromosome) or on both chromosomes of the pair. In a few cases, the mutation is in the mitochondrial rather than the nuclear genome. In any case, the cause is a critical error in the genetic information carried by a single gene. Single-gene disorders usually exhibit obvious and characteristic pedigree patterns. Most such defects are rare, with a frequency that may be as high as 1 in 500 but is usually much less. Although individually rare, as a group single-gene disorders are responsible for a significant proportion of disease and death. Taking the population as a whole, single-gene disorders affect 2 percent of the population sometime over an entire life span. In a population study of more than 1 million live births, the incidence of serious single-gene disorders in the pediatric population was estimated to be 0.36 percent; among hospitalized children, 6 to 8 percent probably have single-gene disorders.

In **chromosome disorders**, the defect is due not to a single mistake in the genetic blueprint but to an excess or a deficiency of the genes contained in whole chromosomes or chromosome segments. For example, the presence of an extra copy of one chromosome, chromosome 21, produces a specific disorder, Down syndrome, even though no individual gene on the chromosome is abnormal. As a group, chromosome disorders are quite common, affecting about 7 per 1000 liveborn infants and accounting for about half of all spontaneous first-trimester abortions.

**Multifactorial inheritance** is responsible for a number of developmental disorders resulting in congenital malformations and for many common disorders of adult life. There appears to be no single error in the genetic information in many of these conditions. Rather, the disease is the result of a combination of small variations in genes that together can produce or predispose to a serious defect, often in concert with environmental factors. Multifactorial disorders tend to recur in families but do not show the characteristic pedigree patterns of single-gene traits. Estimates of the impact of multifactorial disease range from 5 percent in the pediatric population to more than 60 percent in the entire population.

**ONWARD**

During the 40-year professional life of today’s medical and genetic counseling students, extensive changes are likely to take place in appreciating—and acting on—the role of genetics in medicine. It is hard to imagine that any period could encompass changes greater than those seen over the past 50 years, during which the field has gone from first recognizing the
identity of DNA as the active agent of inheritance, to uncovering the molecular structure of DNA and chromosomes, to determining the complete code of the human genome. And yet, judging from the quickening pace of discovery within only the past decade, it is virtually certain that we are just at the beginning of a revolution in integrating knowledge of genetics and the genome into public health and the practice of medicine.

An introduction to the language and concepts of human and medical genetics and an appreciation of the genetic and genomic perspective on health and disease will form a framework for lifelong learning that is part of any health professional's career.

General References